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Haloperidol Oral Solution

General Notices

Haloperidol Oral Drops

Action and use

Dopamine receptor antagonist; neuroleptic.

DEFINITION

Haloperidol Oral Solution is a solution of Haloperidol in a suitable vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

Content of haloperidol, $C_{21}H_{23}ClFNO_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

To a volume containing 20 mg of Haloperidol add 1 mL of 1M *sodium hydroxide* and extract with 10 mL of *dichloromethane*. Filter and evaporate the filtrate to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of haloperidol *(RS 173)*.

TESTS

Acidity

pH, 2.5 to 3.5, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 1 volume of mobile phase A and 9 volumes of mobile phase B (solution A). Prepare the solutions immediately before use and protect from light.

(1) Dilute a volume of the oral solution with sufficient solution A to produce a solution containing 0.01% w/v of Haloperidol.
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.01% w/v of *haloperidol for system suitability EPCRS*.
(4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Hypersil BDS is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 230 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 1.7% w/v of *tetrabutylammonium hydrogen sulfate*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-2	90	10	isocratic
2-17	90→50	10→50	linear gradient
17-22	50	50	isocratic
22-23	50→90	50→10	linear gradient
23-28	90	10	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to haloperidol (retention time about 8 minutes) are: impurity B, about 0.9 and impurity D, about 1.6.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity B and haloperidol is at least 3.0.

LIMITS

Identify any peak corresponding to impurity B in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and multiply the area of this peak by a correction factor of 0.7.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity D is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any peak corresponding to impurity B is not greater than 0.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the area of any other *secondary peak* is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of all *secondary peaks* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

Carry out the method for liquid chromatography, Appendix III D, using the following solutions in a mixture of 1 volume of mobile phase A and 9 volumes of mobile phase B (solution A).

(1) Dilute a volume of the oral solution with sufficient solution A to produce a solution containing 0.005% w/v of Haloperidol.
(2) 0.005% w/v of *haloperidol BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 5 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil ODS is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 247 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

45 volumes of *acetonitrile* and 55 volumes of a 1% w/v solution of *ammonium acetate*.

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{23}ClFNO_2$ in the oral solution using the declared content of $C_{21}H_{23}ClFNO_2$ in *haloperidol BPCRS*.

When Haloperidol Oral Solution or Haloperidol Oral Drops is prescribed or demanded and no strength is stated, an Oral Solution containing 0.2% w/v (2 mg/mL) of Haloperidol shall be dispensed or supplied.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Haloperidol.